The stem cell microenvironment in the maintenance of pluripotency and reprogramming

Grant Award Details

The stem cell microenvironment in the maintenance of pluripotency and reprogramming

Grant Type: Basic Biology I

Grant Number: RB1-01372

Project Objective: The project objective is to interrogate characteristics of subpopulations of cells, and their microenvironment, in cultures of hESC, which are known to be heterogeneous. The goal is to understand how pluripotency is maintained in hESC cultures and how it is established during the reprogramming process.

Investigator:

Name:	Martin Pera
Institution:	University of Southern California
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Cell Line Generation: iPS Cell

Award Value: $1,325,723

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: The stem cell microenvironment in the maintenance of pluripotency and reprogramming

Public Abstract: Pluripotent stem cell research is just on the verge of beginning to fulfill its promise to revolutionize medicine. Whether they are derived from embryos, or from adult cells that have been reprogrammed, human pluripotent stem cells can be propagated indefinitely in the laboratory and can turn into a wide range of mature cell types, providing an renewable source of a wide range of types of human tissue for research or therapy. We are still learning about the best ways to grow and manipulate pluripotent stem cells, and how best to reprogram adult cells to the pluripotent state. In fact, our concept of what a pluripotent stem cell is and what it looks like is still emerging. Recent work has shown that pluripotent stem cells, in the embryo or in the laboratory, are not simply homogeneous monocultures. Rather, stem cell cultures are complex and highly dynamic ecosystems. They contain a spectrum of cell types, from the most primitive cells, to cells that are already well on the way to becoming particular specialized types of cell. Different subpopulations of cells within these ecosystems communicate with one another, and these interactions dictate cell behavior. Cells even produce a type of scaffold on which they grow, called the extracellular matrix, that helps guide its fate. Thus, the microenvironment of the stem cell-its neighbors, and the signaling molecules they produce, is a critical component to guiding the cells fate. Our understanding of this microenvironment is however still rudimentary. This project will study two key processes-stem cell renewal, or the means by which stem cells divide to produce more stem cells, and specification, or how stem cells chose to begin to specialize into more mature cell types. We will look at the regulation of these processes at very high resolution, to see how individual cells within the various subpopulations respond to signals around them, and to identify the critical signals that maintain stem cells in the primitive unspecialized state or help adult cells to become reprogrammed. By carefully dissecting the stem cell population, and identifying its various subcompartments, we will provide critical information for other scientists that will enable them to study stem cell regulation at a much more refined level. And, an enhanced knowledge of the signaling systems cells use to talk to one another will help us to propagate stem cells and to enhance the reprogramming of adult cells. All of these fundamental discoveries will facilitate work towards the application of pluripotent stem cells in medicine.

Statement of Benefit to California: Over the past ten years there has been remarkable progress in human embryonic stem cell research, and much of this progress has been driven in recent times by the California Proposition 71 initiative. Advances in our understanding of stem cell growth and differentiation, the approach of the first clinical trials of human embryonic stem cell derived products, and the remarkable discovery of the reprogramming of adult cells to the pluripotent state, have raised the prospect that this research will soon begin to fulfill its promise to revolutionize medicine. California can take a leading role internationally in this process not only by accelerating the progress of basic discoveries to the clinic, but also by building the intellectual infrastructure for the next decade of discoveries in stem cell research. This proposal is based on a new framework to understand the structure of pluripotent stem cell hierarchies, to unlock the fundamental principles underlying the interaction of pluripotent stem cells with their immediate environment, and to discover how these interactions decide stem cell fate. The results will lead to concrete outcomes in terms of products and processes for stem cell manipulation in research and biotechnology, and they will provide enhanced means for the derivation and propagation of embryonic stem cells and pluripotent stem cells from adult tissues. The basic discoveries will also strengthen the intellectual basis of stem cell research in the State, and the project will provide outstanding training opportunities for California scientists.